REMARKS

This paper is responsive to the Office Action dated August 13, 2003, which is the first action on the merits of the application.

Claims 119-127 were previously pending in the application; claim 127 was withdrawn. Some of the claims are amended, but no claims are added or cancelled. Accordingly, claims 119-126 are now pending in the application and under examination.

Entry of the claim amendments does not introduce new matter into the disclosure. The amendment to claim 119 is supported in the specification on page 116, lines 18-29.

Further consideration and allowance of the application is respectfully requested.

Request for Rejoinder:

Claim 127 is a method claim that depends from and incorporates the limitations of product claim 119. It was presented before any of the claims in this application had been examined in the merits. Applicants hereby request that claim 119 be rejoined into the group under examination, upon determination that the product claims are patentable, in accordance with MPEP § 821.04.

Objection to the Declaration:

Applicants acknowledge the Examiner's request for a new Declaration pursuant to 37 CFR § 1.63. Applicants hereby endeavor to obtain a new executed Declaration from the inventors as requested, or otherwise address this issue.

Written Description

Claims 119-126 stand rejected under 35 USC § 112 ¶ 1 as not being described in the specification in such a way as to convey that the inventors had possession of the invention at the time the application was filed.

The Office Action appears to be missing part of the statements supporting the rejection on page 5. Referring to *Eli Lilly*[1], the Office Action indicates that the claims require a precise definition, such as a structure, formula, chemical name, or physical property. It states that the application does

[1] *Regents of the University of California v. Eli Lilly & Co.*, 43 USPQ2d 1398 (Fed Cir. 1997), *cert. denied*, 510 U.S. 1140 (1994).

not contain a representative number of polynucleotides, and genomic sequences, including introns, 5' untranslated regions, and 3' untranslated regions. It further draws applicants' attention to the *Guidelines for the Examination of Patent Applications,* Federal Register, 66(4), 1099-1111, 2001.

Applicants respectfully submit that the claims as previously presented fully comply with the written description requirements of § 112 ¶ 1. Specifically, the motifs listed in claim 119 provide the structural feature required by *Eli Lilly*. The claim indicates that telomerase proteins falling within the scope will have all of the motifs, and the exemplary species provided in the disclosure show very little variability in the motif structure. Since the claims are defined according to the polypeptides they encode, any introns that may be present, and upstream and downstream untranslated regions are surely not relevant, since these elements have no effect on the encoded protein.

Furthermore, the claims have now been amended to indicate that in addition to the motif structures, the protein should be at least 60% identical to the human TRT sequence on the amino acid level. The claim also requires that the protein have telomerase activity when complexed with telomerase RNA complement.

This combination of structural and functional features complies with the *Guidelines* referred to in the Office Action. Example 14 of the *USPTO Training Materials* for the Written Description Guidelines, Promulgated by the Office on March 7, 2000, is especially helpful. The example shows that a protein defined by a degree of identity with a single representative species, and also by a functional activity, satisfies the written description requirements of § 112 ¶ 1. The claims in the present application exceed this standard by providing not only a degree of sequence identity and a functional activity, but also requiring that the encoded protein have all six of the listed amino acid motifs.

Claims 123-126 stand rejected under 35 USC § 112 ¶ 1 as being new matter not described in the specification as filed.

Applicants respectfully disagree. As indicated in the Amendment filed December 5, 2003, the features referred to in claims 123-125 were taken from Figure 55. Drawings can convey to those of skill in the art that the patentee actually invented what is claimed[2]. Support for TRT fragments of 10 consecutive amino acids or more can be found in the specification *inter alia* on page 16, lines 12-16, and page 46, lines 3-5.

Withdrawal of these rejections is respectfully requested.

Enablement

Claims 119-126 also stand rejected as not being enabled by the specification for the making and using of the full scope of the claimed invention. The Office Action indicates that the specification encompasses a large genus of polynucleotides defined according to motifs present in the encoded protein, but not by the overall structure. It states that the specification does not indicate what alterations in any TRT gene can be made without affecting the functional properties of the encoded protein.

Applicants respectfully disagree. Firstly, the Patent Office has the initial burden to establish a reasonable basis to question the enablement provided for the claimed invention[3]. In making this rejection, the Office has not established that alterations in amino acid structure outside the motifs would adversely affect telomerase catalytic activity. The Office Action indicates that deletion variants lacking the motifs may not have activity, but variants lacking the motifs do not fall within the scope of what is claimed.

Thus, the Office has not established a prima facie case that the structure explicitly required by the claims is not fully sufficient to confer telomerase catalytic activity on any protein encoded by the genus of claimed polynucleotides.

Even if there are other structural aspects of the enzyme that participate in the activity of the enzyme, it is not necessary for these aspects to be recited in the claim if active variants can be found without undue experimentation. The skilled reader will readily recognize that an easy route to TRT

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[2] *Vas-Cath Inc. v. Mahurkar*, 19 USPQ2d 1111, 1116 (Fed. Cir. 1991); *Cooper Cameron Corp. v. Akvaener Oilfield Products, Inc.*, 62 USPQ2d 1846 (Fed. Cir. 2002).

[3] *In re Wright*, 27 USPQW2d 1510 (Fed. Cir. 1993).

variants is to start with one of the exemplary structures given in the specification, make alterations, and empirically determine which alterations retain the desired activity.

Contrary to the assertion in the Office Action, the specification provides considerable guidance as to where to make alterations in the structure when making variants. Specifically, both the specification and the claims guide the reader towards making alterations in the sequence in regions that lie *outside the six claimed motifs*. The claim has now been amended to provide even more guidance to the reader, directing them to create a structure that is homologous to the human TRT sequence (SEQ. ID NO:118).

Although the reader may wish to make variants by mutation at particular sites, it is unnecessary for them to do so. Where the object is only to generate functionally equivalent variants, the skilled reader can employ a random mutation strategy, which is more straightforward and less cumbersome. There is an enormous literature in the art relating to introducing mutations of various kinds. The standard texts *Protocols in Molecular Biology* (Ausubel et al. eds.) and *Molecular Cloning: A Laboratory Manual* (Sambrook et al. eds.) describe techniques employing chemical mutagenesis, cassette mutagenesis, degenerate oligonucleotides, mutually priming oligonucleotides, linker-scanning mutagenesis, alanine-scanning mutagenesis, and error-prone PCR. Other efficient methods include the E. coli mutator strains of Stratagene (Greener et al., Methods Mol. Biol. 57:375, 1996) and the DNA shuffling technique of Maxygen (Patten et al., Curr. Opin. Biotechnol. 8:724, 1997; Harayama, Trends Biotechnol. 16:76, 1998).

The variants can then be cloned out and tested for functionality as described in the specification. Examples 4, 5, and 6 all describe assays for determining telomerase activity, and there were other assays for telomerase known at the time this application was filed: for example, measuring telomere length when TRT is transfected into cells, or measuring extension of telomeric primers by dot blot, reverse transcription, or by the telomerase repeat amplification protocol. The functional variants are selected for use according to the invention, or subjected to further rounds of mutation and functional selection to obtain the degree of variation desired.

The Office Action cites *In re Wands*, 8 USPQ2d (Fed. Cir. 1988) as setting the standard for whether a specification is enabling without undue experimentation. Indeed, the patent under consideration was found to be *enabling* for production of the genus of monoclonal antibodies having the specificity and affinity claimed[4]. The screening of TRT variants for function according to the

[4] In *Wands*, the patent application claimed monoclonal antibodies of a particular specificity and affinity. The PTO contended that only 2.8% of the hybridomas obtained were prov n to fall within the claim, and thus the

present invention is routine in the same manner as testing hybridoma clones for secretion of antibody with particular characteristics.

If the variant has both the required structural features, and the required telomerase catalytic activity, it will fall within the scope of the claimed invention.

Withdrawal of this rejection is respectfully requested.

Rejections under 35 USC § 112 ¶ 2:

Claim 119 and its dependents are rejected as indefinite with respect to SEQ. ID NOs:16 and 17. The amendment made herein to claim 119 is believed to overcome this rejection.

Claim 120 is rejected as indefinite as not being clear whether the structure is an elaboration of a motif from claim 119, or an additional motif that may be present. Applicants respectfully disagree. The reader will understand from Figure 55 and elsewhere in the specification that a TRT polynucleotide according to the claim will typically contain the structure of claim 120 as an elaboration of a motif from claim 119. However, a TRT polynucleotide encoding both structures is not explicitly excluded. Since both possibilities are permitted, no indefiniteness exists.

Claim 121 is rejected as indefinite as not being clear whether SEQ. ID NO:477 is attached to the N- or C-terminus of SEQ. ID NO:16 or 17, or whether there are amino acids in between. Applicants respectfully disagree. The reader will understand from Figure 55 and elsewhere in the specification that SEQ. ID NO:477 is typically concatenated onto the C-terminal of SEQ. ID NO:16 or SEQ. ID NO:17. However, the claim is satisfied by any situation where both sequences occur within the "T" motif. Thus, no indefiniteness exists.

Claims 122-125 are rejected as indefinite as not being clear whether the claimed structures are attached to the terminus of structures in claim 119, or whether there are structures in between. Applicants respectfully disagree. The reader will understand from Figure 55 and elsewhere in the specification that the structures in the dependent claims are typically elaborations of the motif structures in claim 119. However, the claim is satisfied by any situation where both sequences occur within the respective motifs. Thus, no indefiniteness exists.

Claim 126 is rejected as indefinite as not being clear whether the 10 consecutive amino acids recited in the claim are contained within the structures of claim 119, or are elsewhere in the protein.

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claim was not enabled. *The Court held that the application was fully enabled for the claimed subject matter,* because it was standard practice to screen negative hybridomas in order to find one that makes the desired antibody. 8 USPQ2d at 1406-07.

Applicants respectfully disagree. The claim can be satisfied by either of the two alternatives indicated. Accordingly, no indefiniteness exists. Applicants thank the Examiner for noticing that SEQ. ID NO:123 refers to the deletion mutant. The claim has now been amended to refer to full-length TRT (SEQ. ID NO:118).

Withdrawal of these rejections is respectfully requested.

Rejections under 35 USC § 102:

The claims under examination stand rejected under § 102(e) as being anticipated by U.S. Patent 6,029,809, which lists Cech and Lingner as inventors. The invention claimed in the '809 patent is *Euplotes aedicaulatus* TRT (Figure 9, SEQ. ID NO:1). The earliest priority date is October 1, 1996.

Claims 119-126 stand rejected under § 102(e) as being anticipated by U.S. Patent 6,309,867, which lists Cech and Nakamura as inventors. The invention claimed in the '867 patent is *Schizosaccharomyces pombe* TRT ("tez1", Figure 29, SEQ. ID NO:69). The earliest priority date is October 1, 1996.

Claim 119 stands rejected under § 102(a) as being anticipated by GenBank Accession No. U95964, which lists Cech and Lingner as inventors. The Accession No. refers to the article *Science* 276 (5312), 561-567, published in 1997; and a direct submission made on March 31, 1997.

Claim 119 also stands rejected under § 102(a) as being anticipated by an article by Lendvay et al. (Genetics 144:1399, 1996). The Lendvay reference discloses four genes from Saccharomyces cerevisiae, designated EST1, EST2, EST3, and EST4. The reference was apparently published in December of 1996.

None of the cited references qualifies as prior art "by another", for the purposes of supporting a § 102 rejection of the invention claimed here. The present application claims priority to USSN 08/724,643, filed October 1, 1996. This coincides or precedes the priority and publication dates of all the cited references.

The Office Action indicates that the present application is only entitled to a filing date of November 19, 1997. This is incorrect. Benefit of an earlier filing date ensues from 35 USC § 120 if priority is timely claimed to any prior application that shares any one inventor with the present application. Thomas Cech is a common inventor to all the applications and issued patents in this family. Accordingly, this application has a priority date of October 1, 1996, for all the subject matter taught in the October 1, 1996 application (whether claimed or not). Differences between named

inventors in different applications are deliberate, and designed because of the different subject matter claimed in each of the applications.

In order for the Office to establish prior invention under 35 USC §§ 102(a) or 102(e), it must show that there is an embodiment of the claimed invention that was published before a date by which applicants are entitled to the same embodiment in their priority documents. Applicants respectfully submit that no such prior invention exists here.

Withdrawal of these rejections is respectfully requested.

Double patenting rejections:

Claims 119-126 stand rejected under the doctrine of obviousness-type double patenting over U.S. Patent 6,093,809.

Applicants respectfully disagree. Double patenting is considered only with respect to what is claimed in the cited patent, not in what is disclosed. MPEP § 804(II)(B)(1), p. 800-22. The invention claimed in the '809 patent is *Euplotes aedicaulatus* TRT (Figure 9, SEQ. ID NO:1). Claim 119 covers polynucleotides encoding TRT that is at least 60% identical to human TRT (SEQ. ID NO:118).

Figure 55 shows that *Euplotes aedicaulatus* TRT is considerably less than 60% identical to human TRT. Accompanying this Response is a comparison of *Euplotes aedicaulatus* TRT and human TRT using the BLAST algorithm. The comparison confirms that these two TRTs are only about 21% identical at the amino acid level.

Accordingly, the claimed subject matter of the '809 patent do not anticipate claims in the present application. Furthermore, the claimed subject matter of the '809 patent does not suggest how to obtain the subject matter claimed in the present application.

Withdrawal of this rejection is respectfully requested.

Claims 119-126 also stand rejected under the doctrine of obviousness-type double patenting over U.S. Patent 6,261,836.

This rejection is acknowledged. Applicants undertake to file a terminal disclaimer or take other appropriate action upon indication that the application is otherwise in condition for allowance.

Request for Interview

Applicants respectfully request that all outstanding rejections be reconsidered and withdrawn. The application is believed to be in condition for allowance, and a prompt Notice of Allowance is requested.

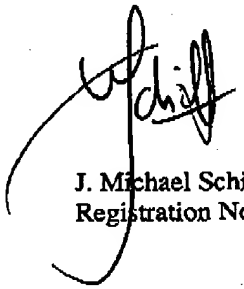
In the event that the Examiner determines that there are other matters to be addressed, applicants hereby request an interview by telephone.

Fees Due

No fee is required with respect to the amendments to the claims.

Should the Patent Office determine that a further extension of time or any other relief is required for further consideration of this application, applicants hereby petition for such relief, and authorize the Commissioner to charge the cost of such petitions and other fees due in connection with the filing of these papers to Deposit Account No. 07-1139, referencing the docket number indicated above.

Respectfully submitted,



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